General

Guideline Title

Clinical practice guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR <45 mL/min).

Bibliographic Source(s)

Guideline development group. Clinical Practice Guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR <45 mL/min). Nephrol Dial Transplant. 2015 May;30 Suppl 2:ii1-142. [343 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The grade for the overall quality of evidence supporting the recommendations (A–D) and the implications of the recommendations (1, 2) are defined at the end of the "Major Recommendations" field.

Note from the National Guideline Clearinghouse: The European Renal Best Practice (ERBP) also provided additional advice for clinical practice. This advice is not graded, elaborates on one or more statements and is intended only to facilitate practical implementation.

Issues Related to Renal Replacement Modality Selection in Patients with Diabetes and End-stage Renal Disease

Should patients with diabetes and chronic kidney disease (CKD) stage 5 start with peritoneal dialysis or haemodialysis (HD) as a first modality?

> The Guideline Development Group (GDG) recommends giving priority to the patient's general status and preference in selecting renal replacement therapy as there is an absence of evidence of superiority of one modality over another in patients with diabetes and CKD stage 5 (1C).
> The GDG recommends providing patients with unbiased information about the different available treatment options (1A).
> In patients opting to start HD, the GDG suggests preferring high flux over low flux when this is available (2C).
> The GDG suggests diabetes has no influence on the choice between HD or haemodiafiltration (HDF) (2B).

Should patients with diabetes and CKD stage 5 start dialysis earlier, i.e., before becoming symptomatic, than patients without diabetes?

The GDG recommends initiating dialysis in patients with diabetes on the same criteria as in patients without diabetes (1A).

In patients with diabetes and CKD stage 5, should a native fistula, graft or tunnelled catheter be preferred as initial access?

- The GDG recommends that reasonable effort be made to avoid tunnelled catheters as primary access in patients with diabetes starting HD as renal replacement therapy (1C).
- The GDG recommends that the advantages, disadvantages and risks of each type of access be discussed with the patient.

Is there a benefit to undergoing renal transplantation for patients with diabetes and CKD stage 5?

The GDG recommends providing education on the different options of transplantation and their expected outcomes for patients with diabetes and CKD stage 4 or 5 who are deemed suitable for transplantation (see Table 5 in the original guideline document) (1D).

Statements Only for Patients with Type 1 Diabetes and CKD Stage 5

- The GDG suggests living donation kidney transplantation or simultaneous pancreas kidney transplantation to improve survival of suitable patients (2C).
- The GDG suggests against islet transplantation after kidney transplantation with the aim to improve survival (2C).
- The GDG suggests pancreas grafting to improve survival after kidney transplantation (2C).

Statements Only for Patients with Type 2 Diabetes and CKD Stage 5

- The GDG recommends against pancreas or simultaneous kidney pancreas transplantation (1D).
- The GDG recommends diabetes in itself should not be considered a contraindication to kidney transplantation in patients who otherwise comply with inclusion and exclusion criteria for transplantation (1C).

Issues Related to Glycaemic Control in Patients with Diabetes and CKD Stage 3b or Higher (Estimated Glomerular Filtration Rate [eGFR] <45 mL/min)

A. Should the aim be to lower glycated haemoglobin (HbA1C) by tighter glycaemic control in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min)?

B. Is an aggressive treatment strategy (in number of injections and controls and follow-up) superior to a more relaxed treatment strategy in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) and using insulin?

- The GDG recommends against tighter glycaemic control if this results in severe hypoglycaemic episodes (1B).
- The GDG recommends vigilant attempts to tighten glycaemic control with the intention to lower HbA1C when values are >8.5% (69 mmol/mol) (1C).
- The GDG suggests vigilant attempts to tighten glycaemic control with the intention to lower HbA1C according to the flow chart in Figure 4 (in the original guideline document) in all other conditions (2D).
- The GDG recommends intense self-monitoring only to avoid hypoglycaemia in patients at high risk for hypoglycaemia (2D).

Are there better alternatives than HbA1c to estimate glycaemic control in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2)?

The GDG recommends the use of HbA1C as a routine reference to assess longer term glycaemic control in patients with CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) (1C).

A. Is any oral drug superior to another in terms of mortality/complications/glycaemic control in patients with diabetes type 2 and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2)?

B. In patients with diabetes type 2 and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2), is maximal oral therapy better than starting/adding insulin at an earlier stage?

- The GDG recommends metformin in a dose adapted to renal function as a first line agent when lifestyle measures alone are insufficient to get HbA1C in the desired range according to Figure 4 in the original guideline document (1B).
- The GDG recommends adding on a drug with a low risk for hypoglycaemia (see Figures 5, 6, and 7 in the original guideline document) as an additional agent when improvement of glycaemic control is deemed appropriate according to Figure 4 in the original guideline document (1B).
- The GDG recommends instructing patients to temporarily withdraw metformin in conditions of pending dehydration, when undergoing contrast media investigations, or in situations with an increased risk for acute kidney injury (AKI) (1C).

Issues Related to Management of Cardiovascular Risk in Patients with Diabetes and CKD Stage 3b or Higher

In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) or on dialysis and with coronary artery disease (CAD), is percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) or conservative treatment to be preferred?

- The GDG recommends not omitting coronary angiography with the sole intention of avoiding potential contrast-related deterioration of kidney function in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) in whom a coronary angiography is indicated (1D).
- The GDG recommends that optimal medical treatment should be considered as preferred treatment in patients with diabetes and CKD stage 3b to stage 5 who have stable CAD, unless there are large areas of ischaemia or significant left main or proximal left anterior descending (LAD) lesions (1C).
- The GDG recommends that when a decision is taken to consider revascularization, CABG is preferred over PCI in patients with multi-vessel or complex (SYNTAX score >22) CAD (1C).
- The GDG recommends that patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) who present with an acute coronary event should be treated no differently than patients with CKD stage 3b or higher (eGFR <45 mL/min) without diabetes or patients with diabetes without CKD stage 3b or higher (eGFR <45 mL/min) (1D).

In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) or on dialysis and with a cardiac indication (heart failure, ischaemic heart disease, hypertension) should inhibitors of the renin-angiotensin-aldosterone system (RAAS) as cardiovascular prevention be prescribed?

- The GDG recommends that adults with CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2 or on dialysis) and diabetes who have a cardiovascular indication (heart failure, ischaemic heart disease) be treated with an angiotensin-converting enzyme inhibitor (ACE-I) at maximally tolerated dose (1B).
- The GDG suggests there is insufficient evidence to justify the start of an angiotensin-receptor blocker (ARB) in adults with CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2 or on dialysis) and diabetes who have a cardiovascular indication (heart failure, ischaemic heart disease) but intolerance for ACE-I (2B).
- The GDG recommends not combining different classes of renin angiotensin-blocking agents (ACE-I, ARBs or direct renin inhibitors) (1A).

In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) or on dialysis, should beta blockers be prescribed to prevent sudden cardiac death?

- The GDG suggests starting a selective beta-blocking agent as primary prevention in patients with diabetes and CKD stage 3b or higher and then continuing it when tolerated (2C).
- The GDG suggests prescribing lipophilic rather than hydrophilic beta-blocking agents in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) (2C).

In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2), should the aim be for lower blood pressure targets than in the general population?

- The GDG suggests against applying lower blood pressure targets in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) than in the general population (2C).
- The GDG suggests that in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) but without proteinuria, all blood pressure-lowering drugs can be used equally to lower blood pressure (2C).

In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2) or on dialysis, should lipid-lowering therapy in primary prevention be prescribed?

- The GDG recommends starting a statin in patients with diabetes and CKD stage 3b and 4 (1B).
- The GDG suggests a statin be considered in patients with diabetes and CKD stage 5 (2C).
- The GDG recommends against starting a statin in patients with diabetes and CKD stage 5d (1A).
- There was no consensus in the GDG on whether or not statins should be stopped in patients with diabetes with CKD stage 5d.
- The GDG suggests fibrates can replace statins in patients with CKD stage 3b who do not tolerate statins (2B).

A. In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2), should interventions aimed at increasing energy expenditure and physical activity be recommended?

B. In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2), should interventions aimed at reducing energy intake be

recommended?

- The GDG suggests that patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) perform additional physical exercise at least three times 1/2 to 1 hour/week to reduce fat mass and improve quality of life (QoL) (2D).
- The GDG suggests that there is no evidence of harm when promoting an individualized regimen of increased physical exercise (2C).
- When promoting weight loss in patients with diabetes and with overweight, the GDG recommends supervision of this process by a dietician and to ensure that only fat mass is lost and malnutrition is avoided (1C).

In patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min/1.73 m^2), should antiplatelet therapy be recommended, regardless of the cardiovascular risk?

- The GDG recommends against adding glycoprotein IIb/IIIa inhibitors to standard care to reduce death, myocardial infarction, or need for coronary revascularization in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) and acute coronary syndromes (ACS) or high-risk coronary artery intervention (1B).
- The GDG suggests not adding a thienopyridine or ticagrelor to standard care to reduce death, myocardial infarction, or need for coronary revascularization in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min) and ACSs or high-risk coronary artery intervention unless there is no additional risk factor for bleeding (2B).
- The GDG recommends starting aspirin as secondary prevention, unless there is a contraindication, side effects or intolerance (1C).
- The GDG suggests starting aspirin as primary prevention only in patients without additional risk factors for major bleeding (2C).

Definitions

Grade for the Overall Quality of Evidence

Grade	Quality Level	Description
A	High	The authors are confident that the true effects lie close to those of the estimates of the effect.
B	Moderate	The true effects are likely to be close to the estimates of the effects, but there is a possibility that they are substantially different.
C	Low	The true effects might be substantially different from the estimates of effects.
D	Very Low	The estimates are very uncertain and will often be far from the truth.

Note: Adapted from Guyatt GH, Oxman AD, Vist GE et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

Implications of the Recommendations

Grade	Implications		
	Patients	Clinicians	Policy
1: Strong, "The GDG recommends"	Most people in your situation would want the recommended course of action, only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be adopted as a policy in most situations.
2: Weak, "The GDG suggests"	Most people in your situation would want the recommended course of action, but many would not.	You should recognize that different choices will be appropriate for different patients. You must help each patient to arrive at a management decision consistent with her or his values and preferences.	Policy-making will require substantial debate and involvement of many stakeholders.

GDG = Guideline Development Group

Note: Adapted from Guyatt GH, Oxman AD, Vist GE et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

The additional category 'ungraded' was used, typically, to provide guidance based on common sense rather than on a systematic literature search. Where applicable, these statements were provided as 'advice for clinical practice'. Typical examples include recommendations regarding monitoring intervals, counselling and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than level 1 or 2 recommendations.

Clinical Algorithm(s)

The following algorithms are available in the original guideline document:

- Decision flow chart for vascular access in patients with diabetes
- Transplantation decision flow chart for patients with type 1 diabetes
- Flowchart of management targets for HbA1C in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min)

Scope

Disease/Condition(s)

- Diabetes mellitus
- Chronic kidney disease (CKD)

Guideline Category

Management

Risk Assessment

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Nephrology

Intended Users

Health Care Providers

Physician Assistants

Physicians

Guideline Objective(s)

- To facilitate informed decision-making on the management of adult individuals with diabetes mellitus and chronic kidney disease (CKD) stage 3b or higher (estimated glomerular filtration rate [eGFR] <45 mL/min)
- To inform about the development of standards of care by policy-makers

Target Population

Adults with diabetes mellitus and chronic kidney disease (CKD) stage 3b or higher (estimated glomerular filtration rate [eGFR] <45 mL/min)

Note: The guideline does not cover interventions in patients with diabetes and CKD stages 1–2 to prevent or delay development of micro- or macro-albuminuria.

Interventions and Practices Considered

1. Provision of patients with unbiased information about different treatment options
2. Renal replacement therapy
    - Haemodialysis (HD)
    - Peritoneal dialysis
    - Haemodiafiltration (HDF)
    - Criteria for initiating renal replacement therapy in patients with diabetes
    - Consideration of access type
3. Renal transplantation
    - Living donation kidney transplantation
    - Simultaneous pancreas kidney transplantation
    - Pancreas grafting to improve survival after kidney transplantation
4. Glycaemic control
    - Glycated haemoglobin (HbA1C) monitoring
    - Lifestyle modification (exercise, weight loss)
    - Oral medication (metformin alone or in combination with additional glycaemia-lowering agents)
5. Management of cardiovascular risk
    - Coronary angiography
    - Percutaneous coronary intervention (PCI)
    - Coronary artery bypass grafting (CABG)
6. Management of patients with a cardiac indication (heart failure, ischaemic heart disease, hypertension) with angiotensin-converting enzyme inhibitors (ACE-I)
7. Management of high blood pressure with beta-blocking agents
8. Lipid-lowering therapy
    - Statins
    - Fibrates
9. Antiplatelet therapy (aspirin, as indicated)

Note: The following were considered but not recommended: islet transplantation after kidney transplantation, combining different classes of renin angiotensin-blocking agents (ACE-I, ARBs or direct renin inhibitors), angiotensin-receptor blockers (ARBs) for people intolerant of ACE-I, lower blood pressure targets in patients with diabetes and chronic kidney disease (CKD) stage 3b or higher than in the general population, adding glycoprotein IIb/IIIa inhibitors to standard care and adding a thienopyridine or ticagrelor to standard care.

Major Outcomes Considered

See Table 1 in the original guideline document for critically important outcomes, highly important outcomes, moderately important (surrogate) outcomes, and question-specific outcomes.

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Development of Clinical Questions

With the final guideline scope as point of departure, the Guideline Development Group (GDG) identified specific research questions for which a systematic review would be conducted. All questions addressed issues related to one of the following three areas:

1. Renal replacement modality selection in patients with diabetes with end-stage renal disease (chronic kidney disease [CKD] stage 5)
2. Glycaemic control in patients with diabetes and CKD stage 3b or higher (estimated glomerular filtration rate [eGFR] <45 mL/min)
3. Management of cardiovascular risk in patients with diabetes and CKD stage 3b or higher (eGFR <45 mL/min)

Development of Review Questions

The methods support team assisted in developing review questions, i.e., framing the clinical questions into a searchable format. This required detailed specification of the patient group (P), intervention (I), comparator (C) and outcomes (O) for intervention questions and the patient group, index tests, reference standard and target conditions for questions of diagnostic test accuracy. For each question, the GDG agreed upon explicit review question criteria including study design features (see Appendices in the original guideline document for detailed review questions and PICO tables).

Searching for Evidence

Sources

The European Renal Best Practice (ERBP) methods support team searched The Cochrane Database of Systematic Reviews (May 2014), The Database of Abstracts of Reviews of Effects (DARE, May 2014), The Cochrane Central Register of Controlled Trials (CENTRAL, May 2014) and Medline (1946 to May, week 4, 2014) for all questions. The search strategies combined subject headings and text words for the patient population, index test and target condition for the diagnostic questions and subject headings and text words for the population and intervention for the intervention questions. The detailed search strategies are available in Appendix 3 in the original guideline document.

Reference lists from the included publications were screened to identify additional papers. The methods support team also searched guideline databases and organizations including the National Guideline Clearinghouse (NGC), Guidelines International Network, Guidelines Finder, Centre for Reviews and Dissemination, National Institute for Health and Care Excellence (NICE) and professional societies of nephrology and endocrinology for guidelines to screen the reference lists.

Selection

For diagnostic questions, the GDG included all studies that compared any of the pre-defined clinical or biochemical tests with a golden standard reference test. For intervention questions, the GDG included all studies in which one of the pre-defined interventions was evaluated in humans. The GDG excluded case series that reported on benefit if the number of participants was ≤5, but included even individual case reports if they reported an adverse event. No restriction was made based on language.

Number of Source Documents

See Appendix 4 in the original guideline document for study selection flow charts.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grade for the Overall Quality of Evidence

Grade	Quality Level	Description
A	High	The authors are confident that the true effects lie close to those of the estimates of the effect.
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Note: Adapted from Guyatt GH, Oxman AD, Vist GE et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Searching for Evidence

Selection

The guideline development group (GDG) used the Early Reference Organisation Software (EROS) (http://www.eros-systematic-review.org) to organize the initial step of screening and selection of papers. The title and abstract of all papers retrieved by the original search were made available to those responsible for screening through this system. For each question, a member of the European Renal Best Practice (ERBP) methods support team and one member of the GDG dedicated to this question independently screened all titles and abstracts and discarded the clearly irrelevant ones and those that did not meet the inclusion criteria. Any discrepancies at this stage were resolved by consensus.

In a second round, full texts of potentially relevant studies were retrieved and independently examined for eligibility and final inclusion in the data extraction step. Any discrepancies were resolved by consensus. If no consensus could be reached, the disagreement was settled by group arbitrage.

The flow of the paper selection is presented for each question in Appendix 4 in the original guideline document.

Data Extraction and Critical Appraisal of Individual Studies

For each included study, the GDG collected relevant information on design, conduct and relevant results through a tailor-made online software system. For each question, two reviewers independently extracted all data. The GDG produced tables displaying the data extraction of both reviewers. Any discrepancies were resolved by consensus, and if no consensus could be reached, disagreements were resolved by a third independent referee. From these data extraction tables, the GDG produced merged consensus evidence tables for informing the recommendations. The evidence tables are available in Appendix 5 in the original guideline document.

Risk of bias of the included studies was evaluated using validated checklists, as recommended by the Cochrane Collaboration. These were AMSTAR for Systematic Reviews, the Cochrane Risk of Bias tool for randomized controlled trials (RCTs), the Newcastle Ottawa scale for cohort and case-control studies and QUADAS for diagnostic test accuracy studies. Data were compiled centrally by the ERBP methods support team.

Evidence Profiles

For research questions regarding therapeutic interventions, the methods support team constructed evidence profiles using the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The evidence profiles include details of the quality assessment as well as summary —pooled or unpooled—outcome data, an absolute measure of intervention effect when appropriate, and the summary of quality of evidence for each outcome. Evidence profiles were reviewed and approved with the rest of the GDG. Evidence profiles were constructed only for research questions addressed by at least two RCTs. If the body of evidence for a particular comparison of interest consisted of only one RCT or of solely observational data, the summary tables provided the final level of synthesis.

Rating the Quality of the Evidence for Each Outcome Across Studies

The GDG rated the overall quality of the evidence for each intervention separately addressing each outcome (see the "Rating Scheme for the Strength of the Evidence" field). In accordance with GRADE, the GDG initially categorized the quality of the evidence for each outcome as high if it originated predominantly from RCTs and as low if it originated from observational studies. The GDG subsequently downgraded the quality of the evidence one or two levels if results from individual studies were at a high or very high risk of bias, there were serious inconsistencies in the results across studies, the evidence was indirect, the data were sparse or imprecise or publication bias was suspected.

The quality of evidence arising from observational studies was upgraded if effect sizes were large, there was evidence of a dose-response gradient, or all plausible confounding would either reduce a demonstrated effect or suggest a spurious effect when results showed no effect (see Table 2 in the original guideline document). Uncontrolled case series and case reports automatically received downgrading from a 'low' to 'very low' level of evidence for risk of bias, so that no other reasons for downgrading were marked.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Establishment of the Guideline Development Group

As defined by the guideline development methodology (see the "Availability of Companion Documents" field), the European Renal Best Practice (ERBP) advisory board installed a steering group, which, after selection of the topics, selected further members for the guide- line development group. Members of the steering group and the Guideline Development Group (GDG) were selected based on their clinical and research expertise and their willingness to invest the necessary time and effort to perform the task according to the proposed deadlines and the agreed methodology. The GDG consisted of content experts, including individuals with expertise in endocrinology and diabetes, general internal medicine and clinical nephrology. In addition, experts in epidemiology and systematic review methodology were added to the GDG. The ERBP methods support team provided methodological input and practical assistance throughout the process.

Formulating and Grading Statements

Statements

After the evidence tables and profiles had been prepared, revised and approved, the GDG formulated and graded the statements during two full-day plenary meetings.

Recommendations can be for or against a certain strategy. The GDG drafted the statements based on their interpretation of the available evidence. Individual statements were made and discussed in an attempt to reach group consensus. If the GDG could not reach consensus, a formal open vote by show of hands was held. An arbitrary 80% had to cast a positive vote for a statement to be accepted. Voting results and reasons for disagreement were specified in the rationale where applicable. In accordance to Grading of Recommendations Assessment, Development and Evaluation (GRADE), the GDG classified the strength of the statements as strong or weak (see the "Rating Scheme for the Strength of the Recommendations" field and Figure 1 in the original guideline document).

Judgements around four key factors determined the strength of a recommendation: the balance between desirable and undesirable consequences of alternative therapeutic or diagnostic strategies, the quality of the evidence and the variability in values and preferences.

Ungraded Statements

The GDG decided to use an additional category of ungraded statements for areas where formal evidence was not sought and statements were based on common sense, or expert experience alone. The ungraded statements were generally written as simple declarative statements but were not intended to be stronger than level 1 or 2 recommendations.

Rating Scheme for the Strength of the Recommendations

Implications of the Recommendations

Grade	Implications		
	Patients	**Clinicians**	**Policy**
1: Strong, "The GDG recommends"	Most people in your situation would want the recommended course of action, only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be adopted as a policy in most situations.
2: Weak,	Most people in your situation	You should recognize that different choices will be	Policy-making will

Grade	Patients	Implications Clinicians	Policy
"The GDG suggests"	would want the recommended course of action, but many would not.	appropriate for different patients. You must help each patient to arrive at a management decision consistent with her or his values and preferences.	require substantial debate and involvement of many stakeholders.

GDG = Guideline Development Group

Note: Adapted from Guyatt GH, Oxman AD, Vist GE et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

The additional category 'ungraded' was used, typically, to provide guidance based on common sense rather than on a systematic literature search. Where applicable, these statements were provided as 'advice for clinical practice'. Typical examples include recommendations regarding monitoring intervals, counselling and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than level 1 or 2 recommendations.

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal and External Review

Internal Review

A first draft of the guideline was sent to internal reviewers from the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) council and the European Renal Best Practice (ERBP) advisory board. Internal reviewers were asked to comment on the statements and the rationale within free text fields. All these comments and suggestions were discussed during an ERBP advisory board meeting, during a meeting of the ERBP methods support team, and during an additional teleconference meeting of the Guideline Development Group (GDG). For each comment or suggestion, the GDG evaluated whether the statement needed to be adapted, again taking into account the balance between desirable and undesirable consequences of the alternative management strategies, the quality of the evidence, and the variability in values and preferences.

External Review

The guideline was sent to the Endocrine Society of Australia (ESA), the European Society of Endocrinology, Kidney Health Australia–Caring for Australasians with Renal Impairment (KHA-CARI) and the American Society of Nephrology (ASN), with the request to have the guideline evaluated by two of their members.

In addition, all members of the ERA-EDTA received an online questionnaire in Survey Monkey format to evaluate the guideline using the Appraisal of Guidelines for Research and Evaluation (AGREE)-II framework. In addition, a free text field was provided to allow for additional comments.

All comments and suggestions were discussed with the GDG by e-mail, as well as during a final meeting of the co-chairs of the GDG, the methods support team and the chair of ERBP.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with diabetes and chronic kidney disease (CKD) stage 3b or higher (estimated glomerular filtration rate [eGFR] <45 mL/min)

See the "Rationale" sections in the original guideline document for benefits of specific interventions.

Potential Harms

Adverse effects associated with treatment

See the "Rationale" sections in the original guideline document for harms of specific interventions.

Qualifying Statements

Qualifying Statements

This clinical practice guideline was designed to facilitate informed decision-making on the management of adult individuals with diabetes mellitus and chronic kidney disease (CKD) stage 3b or higher (estimated glomerular filtration rate [eGFR] <45 mL/min). It was not intended to define a standard of care, and should not be construed as such. It should not be interpreted as a prescription for an exclusive course of management.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Guideline development group. Clinical Practice Guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR <45 mL/min). Nephrol Dial Transplant. 2015 May;30 Suppl 2:ii1-142. [343 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 May

Guideline Developer(s)

European Renal Best Practice - Independent Expert Panel

Source(s) of Funding

The European Renal Best Practice (ERBP) sponsored the entire production of this guideline, according to the statutes of the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) and the bylaws of ERBP.

Activities of ERBP and its methods support team are supervised by an advisory board (see www.european-renal-best-practice.org for details and declaration of interests). ERBP is an independent part of ERA-EDTA. The council of ERA-EDTA approves and provides the annual budget based on a proposition made by the ERBP chair. ERA-EDTA receives money and is partly funded by industrial partners, but its council is not involved with and does not interfere with question development or any other part of the guideline development process. The Guideline Development Group (GDG) did not receive any funds directly from industry to produce this guideline.

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

All members of the Guideline Development Group (GDG) were required to complete a detailed 'declaration of interest statement' including all current and future conflicts of interest as well as past conflicts of interest restricted to 2 years before joining the GDG. European Renal Best Practice (ERBP) felt that excluding all individuals with some degree of potential conflict of interest would prevent the assembly of a GDG. The authors therefore allowed members of the GDG to have past financial and/or intellectual conflicts of interest. No consequences were attached to the stated interests, but rather the authors insisted on transparency. All members of the GDG were allowed to participate in all discussions and had equal weight in formulating the statements. All were allowed equal involvement in data extraction and writing the rationales.

The declaration of interest forms are available from http://www.european-renal-best-practice.org/content/ERBP-Workgroup-Diabetes-0 and are updated on a regular basis. They can also be found in Appendix 1 in the original guideline document.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Nephrology Dialysis Transplantation Journal Web site.

Availability of Companion Documents

The following are available:

- Clinical practice guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR <45 mL/min). Supplementary data. 2015 May. 277 p. Available from the Nephrology Dialysis Transplantation Journal Web site.
- Nagler EV, Webster AC, Bolignano D, Haller MC, Nistor I, van der Veer SN, Fouque D, Van Biesen W. European Renal Best Practice (ERBP) guideline development methodology: towards the best possible guidelines. Nephrol Dial Transplant 2014 Apr;29(4):731–8. Available from the Nephrology Dialysis Transplantation Journal Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on September 17, 2015. The information was verified by the guideline developer on November 11, 2015. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs.

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